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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/463,209	BERGHOF ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-65 and 67-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-65 and 67-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/3/04 has been entered.

2. Claims 52, 53, 54, 56, 57, 58, 64, 65, 67, 68, and 69 are amended, claim 66 is cancelled and claims 70-81 have been added. Claims 52-65 and 67-81 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. New rejections are set forth to address the amended and added claims.

4. Applicant is reminded that SEQ ID NO: 5 as recited in claim 69 is withdrawn from prosecution as being non-elected. Claim 69 was examined only insofar as it recites SEQ ID NO: 3 and SEQ ID NO: 4. Reference to SEQ ID NO: 5 in claim 69 should be removed.

5. The drawings are approved with regard to formal matters. However, as noted below, the are objected to as containing new matter.

Sequence Rules

6. The sequence listing filed 3/3/2004 is entered into the application. The CRF filed therewith has been entered into the STIC database. This application is in compliance with the sequence rules.

Specification

7. The new matter objection is withdrawn in view of the cancellation of the drawings in the paper filed 3/3/04 and the amendment of the sequence listing to remove the sequences that were previously considered new matter.

Claim Rejections - 35 USC § 112

New Matter

8. Claims 52-65 and 67-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In claims 52-65 and 67-69, the new limitation of "to not hybridize to and/or amplify RNA or DNA of non-*Staphylococcus aureus* bacterial species" in claims 52, 53, 54, 58, 67, 68, and 69 appears to represent new matter. Claims 55-57 and 59-66 each contain this limitation by virtue of their dependence from claims that specifically recite the limitation. No specific basis for this limitation was identified in applicant's paper, nor did a review of the specification by the examiner find any basis for the limitation. Specifically, the exclusion proviso in which the probe

is designed not to hybridize to the entire group of "non- *Staphylococcus aureus* bacterial species" is not found in the specification. As noted by MPEP 2173.05(i),

> "Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

Since no basis has been identified, the claims are rejected as incorporating new matter.

In claims 70-81, the addition of control nucleic acids, both positive and negative, to the claimed kits appears to represent new matter. The response refers to Example 1 for basis for the limitations. While Example 1 does demonstrate the use of many different nucleic acids in hybridization assays for the testing of probes, Example 1 does not discuss positive or negative controls, per se. Further, and more to the point, Example 1 does not discuss the inclusion of any of these molecules in kits for the analytical detection of Stapphylococcus. The specification appears to only discuss the contents of kits in one place, on page 10 in the third paragraph, wherein it states that such a kit would be characterized by "one or more nucleic acid molecules according to the invention." The specification does not appear to contemplate the inclusion of control molecules in the kits of the invention. Since no basis has been identified, the claims are rejected as incorporating new matter.

First Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 52-65 and 67-81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims are drawn to a nucleic acids as well as kits for the analytical detection of Staphylococcus aureus which comprise nucleic acid probes and/or primers.

Claim 52 minimally requires that at least one probe in the kit comprises 10 successive nucleotides of the region comprising position 54 to 83 of SEQ ID NO: 1 or nucleotide positions 100-166 of SEQ ID NO: 1, and that the sequence be able to selectively hybridize to RNA or DNA of S. aureus and not to non-S. aureus bacterial species. Claim 53 does not set forth any structural requirement for the probes in the claimed kit, merely requires that they be able to hybridize to or amplify S. aureus and distinguish between S. aureus and a non-S. aureus bacteria that differs by at least one base pair in SEQ ID NO: 1. The claim does not further define the "bacteria not to be detected." Claim 54 is similar to claim 53 but delineates specific regions of SEQ ID NO: 1 where the one base pair difference must occur. Claim 55 recites that the kit comprise a nucleic acid probe that "comprises" SEQ ID NO: 1. Claims 56-57 require that the kit of claim 54 comprise smaller sequences that are portions of SEQ ID NO: 1. Claim 58 recites probes that have only 8 or 9 successive nucleotides of portions of SEQ ID NO: 1 or are 90% homologous to portions of SEQ ID NO: 1. Claims 59-65 depend from one of the previous claims and provide modifications via the addition of labels or nucleotide changes. Claims 67-69 are directed towards probes that comprise SEQ ID NO: 1 or portions of SEQ ID NO: 1. The genus encompassed within the instant claims is quite large, encompassing nucleic acids that have

fragments of SEQ ID NO: 1 embedded in any framework, as well for claim 53-54 any possible nucleic acid that would meet the functional limitations of the claims, as the claim does not even require that the claimed nucleic acid encompass SEQ ID NO: 1 or portions thereof. Claims 70-81 are kit claims which contain the same probes but additionally have nucleic acid controls.

The specification provides a nucleic acid consisting of SEQ ID NO: 1, and identifies specific regions of SEQ ID NO: 1 have high variability compared to other Staphylococcal species, and are therefore useful for determining species specific probes (p. 15). SEQ ID NO: 1 is from the species S. aureus. The specification does not provide the sequence corresponding to SEQ ID NO: 1 for any other species. Thus, the specification does not provide guidance as to how SEQ ID NO: 1 can be modified but still retain the functional properties recited in the claims. Each of the claims is drawn using "comprising" language, and therefore encompass fragments of SEQ ID NO: 1 within any other sequence, provided the nucleic acids meet the functional requirements of the claims. However, no description is provided of sequences other than those consisting of instant SEQ ID NO: 1 and consisting of fragments of instant SEQ ID NO: 1.

The specification provides no guidance as to what differences between in SEQ ID NO: 1 and some other sequence would be useful for distinguishing between bacteria to be detected and not to be detected. This genus of bacteria not to be detected in enormous given all ofhte different types of bacteria known. Thus, applicant has express possession of a limited number of species (a probe consisting of SEQ ID NO: 1, as well as probes which consist of fragments of SEQ ID NO: 1) in a genus which comprises hundreds of millions of different possibilities. It is noted that from within this single exemplified sequence three additional probes are given, named as SEQ ID NO: 2-4. These are also considered to be properly described.

With regard to the written description, many of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, include modifications by permitted by the % identity language as well as for "base pair differences" for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic acids of the disclosed SEQ ID Nos are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids modified by addition, insertion, deletion, substitution or inversion with the disclosed SEQ ID No: 1 but possessing one such that a different nucleic acid sequence is retains S. aureus detecting function or such that the nucleic acid has the ability to detect other species of Staphylococcus.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 52-63 and 67-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Kunsch *et al.* (CA 2194411).

This document is a "laid open" Canadian patent application. When the application is "laid open" all parts of the application as filed become available to the public. In the instant case, the Canadian patent office did not publish the sequence listing for CA 2194411 A1. However, the full sequence listing was available to the public on the day the application was laid open. It is assumed that this sequence listing is identical to that in the CA 2194411 A1 application.

Kunsch *et al.* teach kits comprising at least one nucleic acid probe, wherein at least one of the nucleic acid molecules hybridizes selectively to the RNA or DNA of S. aureus. Kunsch *et al.* provide, in 5,191 sequences, polynucleotides of the genome of S. aureus (p. 7). Kunsch *et al.* teach fragments that can be used to diagnose S. aureus (DF's) (p. 8, line 8) and kits which comprise these fragments (p. 42, line 24-p. 44, line 12). Many of the sequences taught by Kunsch *et al.* meet the limitations of the instant claims.

For example, SEQ ID NO: 3803 taught by Kunsch *et al.* comprises SEQ ID NO: 1. Instant SEQ ID NO: 1 is the complement of 26-196 of Kunsch *et al.*'s SEQ ID NO: 3803.

As another example, SEQ ID NO: 4725 taught by Kunsch *et al.* comprises part of nucleotides 54-83 of instant SEQ ID NO: 1. Nucleotides 106-134 of SEQ ID NO: 4725 are identical to nucleotides 54-82 of SEQ ID NO: 1. Therefore, SEQ ID NO: 4725 also comprises SEQ ID NO: 2.

As a third example, SEQ ID NO: 5094 taught by Kunsch *et al.* comprises nucleotides 100-166 of instant SEQ ID NO: 1, but is shorter than instant SEQ ID NO: 1. Kunsch *et al.*'s SEQ ID NO: 5094 consists of 51 nucleic acids which are identical to nucleotides 83-135 of instant SEQ ID NO: 1. Therefore, SEQ ID NO: 5094 also comprises SEQ ID NO: 4 which are found at positions 102-121 of SEQ ID NO: 1.

These sequences would hybridize selectively to S. aureus, and each contain at least ten nucleotides from position 54 to 83 of SEQ ID NO: 1, or position 100 to 166 of SEQ ID NO: 1, or sequence complementary to these regions. These sequences could be used to distinguish between S. aureus and other sequences via a hybridization assay. At least one of these sequences "has" (i.e. comprises) instant SEQ ID NO: 1.

Kunsch *et al.* provide many additional nucleic acids whose sequences meet the limitations of at least one, if not all, of the rejected claims. Specific identification of these nucleic acids would have been duplicative of the three mentioned examples.

Claim 52 requires that the kit comprise at least on nucleic acid molecule primer or probe that is comprised of at least 10 successive nucleotides of the region comprising nucleotide position 54 to 83 of SEQ ID NO: 1 or nucleotide position 100-166 of SEQ ID NO: 1. The meets this structural limitation of the claim, as SEQ ID NO: 3803 taught by Kunsch *et al.* comprises all of SEQ ID NO: 1 and thus comprises both of these portions in their entirety. The limitations of the claim which recite that the primer and/or probe is adapted for to hybridize to or amplify S. aureus DNA and not "non- *Staphylococcus aureus* bacterial species" is intended use language. The probe taught by Kunsch *et al.* appears to meet this limitation of the claim as it is a particular portion of S. aureus DNA which comprises instant SEQ ID NO: 1. This probe would be

expected to not hybridize to at non-*Staphylococcus aureus* bacterial species under highly stringent hybridization conditions, at least. This is an inherent property of the probe.

With regard to claims 53, 54, 55, 56 and 57, at least one of the probes taught by Kunsch *et al.* is considered to be adapted to selectively hybridize and/or amplify RNA or DNA from *S. aureus* as they are all fragments of the *S. aureus* genome, and further the probes taught by Kunsch *et al.* are "adapted to" distinguish between bacteria to be detected and bacteria not to be detected by a differing nucleic acid sequence it at least one base position in SEQ ID NO: 1 in the genomic DNA and/or RNA of said bacteria to be detected and said bacteria not to be detected. A nucleic acid comprising SEQ ID NO: 1 would be adapted to distinguish between SEQ ID NO: 1 and a sequence that differs from SEQ ID NO: 1 by at least one nucleotide. Kunsch *et al.* teach such a molecule. This applies to claim 56 because the recited positions within the claim are contained within SEQ ID NO: 1. This applies to claim 57 because each of SEQ ID NO: 2, 3, and 4 are portions of SEQ ID NO: 1. Claims 56 and 57 depend from claim 55, and thus must include all of the limitations of claim 55 which requires that the probe comprises SEQ ID NO: 1 in its entirety.

With regard to claim 58, SEQ ID NO: 3803 taught by Kunsch *et al.* comprises 9 out of 10 successive nucleotides of the recited portions of SEQ ID NO: 1, as the sequence comprises SEQ ID NO: 1 in its entirety.

With regard to claim 59, Kunsch *et al.* teach that the nucleic acids of their invention include both single and double stranded molecules (p. 19, lines 21-22).

With regard to claim 60, the molecules taught by Kunsch *et al.* are DNA or RNA (p. 19, lines 21-22).

With regard to claims 61-63, all nucleic acid molecules, including those taught by Kunsch *et al.* comprise groups for an indirect or direct reaction, provided the proper reacting partners are present. For example, nucleic acids can be extended or cleaved, which would be encompassed within such reactions, and would also be enzymatic reactions (claim 62) that utilize an enzyme (claim 63).

With regard to claim 67, the molecules taught by Kunsch *et al.* include a nucleotide probe comprising SEQ ID NO: 1. The nucleic acid taught by Kunsch *et al.* as SEQ ID NO: 3803 is a nucleic acid comprising SEQ ID NO: 1. With regard to claim 68, this nucleic acid molecule comprises positions 54 to 83 of SEQ ID NO: 1 and nucleotide positions 100-166 of SEQ ID NO: 1 as it comprises SEQ ID NO: 1 in its entirety, and thus also comprises all portions of SEQ ID NO: 1. With regard to claim 69, Kunsch *et al.* teach a nucleotide probe having SEQ ID NO: 3 and SEQ ID NO: 4, as these are all also fragments of SEQ ID NO: 1, which Kunsch *et al.* teach in its entirety.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 64-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kunsch *et al.* in view of Buchardt *et al.* (Trends in Biotechnology, 1993, 11(9), 384-386).

Kunsch *et al.* teach kits comprising more than one nucleic acid probes, wherein at least one of the nucleic acid molecules hybridizes selectively to the RNA or DNA of S. aureus. Kunsch *et al.* provide, in 5,191 sequences, polynucleotides of the genome of S. aureus (p. 7). Kunsch *et al.* teach fragments that can be used to diagnose S. aureus (DF's) (p. 8, line 8) and kits which comprise these fragments (p. 42, line 24-p. 44, line 12). Many of the sequences taught by Kunsch *et al.* meet the limitations of the instant claims.

For example, SEQ ID NO: 3803 taught by Kunsch *et al.* comprises SEQ ID NO: 1. Instant SEQ ID NO: 1 is the complement of 26-196 of Kunsch *et al.*'s SEQ ID NO: 3803. Thus, at least one of the nucleic acid molecules taught by Kunsch *et al.* is comprised of at least 10 successive nucleotides of the region comprising nucleotide position 54 to 83 of SEQ ID NO: 1 and nucleotide position 100 to 166 of SEQ ID NO: 1, as SEQ ID NO: 3803 taught by Kunsch *et al.* comprises all of SEQ ID NO: 1 and thus comprises both of these portions.

Kunsch *et al.* do not discuss nucleotides that are not naturally occurring in bacteria.

Buchardt *et al.* teach that peptide nucleic acid probes are resistant to nuclease cleavage and protease attack and are promising as biomolecular and diagnostic probes (ABSTRACT, for example). Peptide nucleic acids are made up of "analogous nucleotides" that are not naturally occurring in bacteria.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the detection fragment taught by Kunsch *et al.* so as to have used PNA instead of DNA as a detection fragment, thereby to have replace all of the sequence of the probe with peptide nucleic acid, in order to obtain the benefits of using a PNA probe as taught by Buchardt. Such a modification would have encompassed modifying 10% of the probe and 1 or two nucleotides of the probe. Indeed modifying the entire detection fragment encompasses both 10% and 1 or 2 nucleotides as recited in claims 64 and 65.

16. Claims 70-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kunsch *et al.* in view of both Bergeron *et al.* (US 5994066) and Shah *et al.* (US 5370992).

Kunsch *et al.* teach a kit comprising at least one nucleic acid probe, wherein at least one of the nucleic acid molecules hybridizes selectively to the RNA or DNA of S. aureus. Kunsch *et al.* provide, in 5,191 sequences, polynucleotides of the genome of S. aureus (p. 7). Kunsch *et al.* teach fragments that can be used to diagnose S. aureus (DF's) (p. 8, line 8) and kits which comprise these fragments (p. 42, line 24-p. 44, line 12). Many of the sequences taught by Kunsch *et al.* meet the probe limitations of the instant claims. For example, SEQ ID NO: 3803 taught by Kunsch *et al.* comprises SEQ ID NO: 1. Instant SEQ ID NO: 1 is the complement of 26-196 of Kunsch *et al.*'s SEQ ID NO: 3803.

With regard to claims 70 and 76, SEQ ID NO: 3803 taught by Kunsch *et al.* is designed to hybridize with the complement of instant SEQ ID NO: 1.

With regard to claims 71 and 77, SEQ ID NO: 3803 taught by Kunsch *et al.* is designed to hybridize with the complement of both nucleotides 54-83 and nucleotides 100-166 of SEQ ID

NO: 1, as this probe comprises SEQ ID NO: 1 in its entirety, therefore it comprises these regions as well.

With regard to claim 72 and 78, SEQ ID NO: 3803 taught by Kunsch *et al.* is designed to hybridize with the complement of each of SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4 each of these are comprised within instant SEQ ID NO: 1 which is comprised within the sequence taught by Kunsch *et al.*

With regard to claim 73 and 79, SEQ ID NO: 3803 taught by Kunsch *et al.* comprises SEQ ID NO: 1.

With regard to claim 74 and 80, SEQ ID NO: 3803 taught by Kunsch *et al.* comprises SEQ ID NO: 1, therefore it comprises both of the portions of SEQ ID NO: 1 listed in claim 74.

With regard to claim 75 and 81, SEQ ID NO: 3803 taught by Kunsch *et al.* comprises each of SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4, as these are all fragments of SEQ ID NO: 1 which is comprised in its entirety within SEQ ID NO: 3803 taught by Kunsch *et al.*

Kunsch *et al.* do not teach a kit which comprises a negative control nucleic acid isolated from a non-*Staphylococcus aureus* bacterial species or a positive control nucleic acid isolated from a *Staphylococcus aureus* bacterial species.

However, the inclusion of negative controls in kits for the detection of particular molecules or organisms was routine in the prior art at the time the invention was made. Bergeron *et al.* teach a kit for the detection of bacteria in biological samples and teach that "[o]f course, the kit will include standard samples to be used as negative and positive controls for each hybridization test (Example 15, Col. 21, lines 30-34)." Furthermore, Shah *et al.* exemplify hybridization methods for the detection of *Y. enterocolitica*, and utilize nucleic acids from non-*Y.*

enterocolitica bacteria as negative control (Col. 10, lines 53-55), thus demonstrating that for a given bacteria, an appropriate negative control would be DNA different bacteria. Shah *et al.* further use *Y. enterocolitica* as a positive control, indicated by a "(c)" in table 2, against which all other hybridization strengths are measured. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the kit taught by Kunsch *et al.* so as to have included a negative control nucleic acid isolated from a non-*Staphylococcus aureus* bacterial species and a positive control nucleic acid from a *Staphylococcus aureus* bacterial species. One would have been motivated to include a control in the kits for the detection of *S. aureus* in order to have provided practitioners utilizing the kits with a means for testing the assay to ensure the integrity of the assay for which the kits would be used.

Response to Remarks

The 112 2nd rejections are withdrawn in view of the amendments to the claims which overcome the 112 2nd rejections.

The rejection under Written Description is maintained over the amended claims and applied to the newly filed claims. Applicants traverse the rejection. Applicant points out that the present invention teaches that primers and/or probes desigened to bind to a region comprising only 0.002% of the genome of S. aureus can be used for the specific detection of S. aureus strains. This is not disputes. Applicnat's claims, however encompass probes and primers that are not necessarily portions of SEQ ID NO: 1, the region of the genome that applicant has described as having this ability, due to the use of the broad "comprising" and "hybridization" and "homology" language of the claims. Applicants have not demonstrated possession of such a

broad genus, as noted in the rejection, applicants have only demonstrated possession of a nucleic acid consisting of SEQ ID NO: 1 and consisting of fragments of SEQ ID NO: 1. The rejection is maintained.

Applicants traverse the 102(b) rejection in view of Kunsch *et al.* stating that Kunsch *et al.* fail to provide any teaching about which regions within the 8 million base pair genomic sequence are sufficiently conserved between all strains of S. aureus, but are sufficiently diverbent from the sequences of other bacterial species to be useful for the unequivocal detection of all S. aureus. However, this is irrelevant. Kunsch *et al.* teach products that meet the structural and functional limitations of the instant claims, as discussed in the rejections. The recitation that Applicants argue are missing from Kunsch *et al.* are directed towards applicant's intended use of the claimed invention. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In the instant case, the isolated nucleic acid probes and primers taught by Kunsch *et al.* are no different from the instantly claimed nucleic acid molecule (see MPEP 2111.02). The rejection is therefore maintained.

Applicant traverses the rejection under 103 on the same grounds as the traversal of the 102. For the same reasons, then, the rejection is maintained.

New rejections are set forth to address the newly added claims.

Conclusion

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Green *et al.* (GenBank L36472, 11 November 1994) provide a nucleic acid sequence which comprises the 5s-23s spacer region of Staphylococcus aureus. The sequence taught by Green *et al.* comprises instant SEQ ID NO: 1.

18. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Juliet C Switzer
Examiner
Art Unit 1634

May 5, 2004